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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,615	12/04/2003	Vivek M. Rangnekar	028750-225	5759
23911 7590 11/26/2008 CROWELL & MORING LLP INTELLECTUAL PROPERTY GROUP P.O. BOX 14300 WASHINGTON, DC 20044-4300				
EXAMINER MARVICH, MARIA				
ART UNIT		PAPER NUMBER		
1633				
MAIL DATE		DELIVERY MODE		
11/26/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/726,615

**Applicant(s)**

RANGNEKAR, VIVEK M.

**Examiner**

MARIA B. MARVICH

**Art Unit**

1633

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 6-8, 10, 11 and 18-24 is/are pending in the application.
- 4a) Of the above claim(s) 7, 8, 10, 11 and 18-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 6 and 24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 6/9/08
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/9/08 has been entered.

Claims 1, 6-8, 10, 11 and 18-24 are pending. Claims 7, 8, 10, 11 and 18-23 are withdrawn. Therefore, claims 1, 6 and 24 are under examination in this application.

#### ***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 6 and 24 are drawn to an isolated rat prostate apoptosis responsive 4 protein fragment selected from the group consisting of 1-204, 137-221, 137-213, 137-198 and 137-195 of rat PAR-4. The sequence is not provided although the specification teaches, "The Par-4 gene, first identified by the inventors (see Sells et al., 1994) in prostate cancer cells undergoing

apoptosis, encodes a proapoptotic protein that is remarkably effective in inducing cancer cell apoptosis and tumor regression in animal models". A review of this document reveals that this sequence corresponds to UO5089.1. Hence, applicants have disclosed a single species of rat PAR-4 sequences and isolation of fragments thereof that can mediate reduction of tumor size in apoptosis resistance tumors. The written description requirement under 35 USC 112, first paragraph may be met by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at [www.uspto.gov](http://www.uspto.gov)).

In this case, the claims are drawn to a genus of sequences for which applicants have provided disclosure of a single species. Structurally, the nomenclature 1-204, 137-221, 137-213, 137-198 and 137-195 translates into peptides that have been deleted of all but a core region applicants have identified as a death domain in rat protein. Hence, rat Par-4 comprises a unique core domain that is 59 amino acids that comprises a nuclear localization domain and two phosphorylation sites that are localized to between position 137 and 195 of "the wild-type rat Par-4" protein. This region contains a nuclear localization sequence, which is sufficient and necessary to induce apoptosis in Par-4 resistant cancer cells as well as Gas pro death pathway activation. Par-4 mutants deleted of the nuclear localization signal at 147-153 did not enter the nucleus and did not lead to apoptosis of PC3 cells. And Par-4 mutants 1-204, 137-221, 137-213,

137-198 and 137-195 lead to apoptosis in transient transfections in several cancer cells but not the corresponding normal cells. A panel of androgen dependent or independent prostate cancer cells, immortalized cells and primary cells were tested. Apoptosis was induced in androgen dependent and independent cells but not the normal or immortalized cells (see Table 1 and 2).

However, it is not clear what amino acid numbers corresponding to 1-204, 137-221, 137-213, 137-198 and 137-195 for example in allelic variants correspond. The nature of alleles is that they are of variant structure often with mutations, the structure of one does not provide guidance to the structure of others and the common attributes are not described in the specification. There is no indication of how the structure of one allele is representative of unknown alleles. Given the recitation to specific deletion mutants, 1-204, 137-221, 137-213, 137-198 and 137-195, without providing a reference sequence engenders a level of difficulty in identifying the proper "core" that is meant to be contained within 1-204, 137-221, 137-213, 137-198 and 137-195 in other variants. These positions become artificial landmarks without an indication as to what sequences can or are contained within them. The specification teaches that the particular Par-4 peptide of the instant invention has 332 amino acids and the modified peptide must comprise 1-204, 137-221, 137-213, 137-198 and 137-195, it is highly unpredictable that the sequences corresponding to 1-204, 137-221, 137-213, 137-198 and 137-195 can be identified for any Par-4 peptide given the wide and variable sequences known as Par-4. Given the unknown size and nature of the recited source protein and the inability to determine if there are others that also possess the ability to encode a death domain within the exact recited amino acids, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of full length and JNK binding fragments would not represent to the skilled artisan

a representative number of species sufficient to show applicants were in possession of claimed genus.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD  
Primary Examiner  
Art Unit 1633

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